

*2nd time*

10726550a.trn

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1626GMS

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS	4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS	5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS	6	NOV 10	CA/Capplus F-Term thesaurus enhanced
NEWS	7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS	8	NOV 20	CA/Capplus to MARPAT accession number crossover limit increased to 50,000
NEWS	9	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS	10	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS	11	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS	12	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS	13	DEC 18	CA/Capplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS	14	DEC 18	CA/Capplus patent kind codes updated
NEWS	15	DEC 18	MARPAT to CA/Capplus accession number crossover limit increased to 50,000
NEWS	16	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS	17	DEC 27	CA/Capplus enhanced with more pre-1907 records
NEWS	18	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	19	JAN 16	CA/Capplus Company Name Thesaurus enhanced and reloaded
NEWS	20	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	21	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	22	JAN 22	CA/Capplus updated with revised CAS roles
NEWS	23	JAN 22	CA/Capplus enhanced with patent applications from India
NEWS	24	JAN 29	PHAR reloaded with new search and display fields
NEWS	25	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	26	FEB 13	CASREACT coverage to be extended
NEWS	27	Feb 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	28	Feb 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	29	Feb 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	30	Feb 26	MEDLINE reloaded with enhancements
NEWS	31	Feb 26	EMBASE enhanced with Clinical Trial Number field
NEWS	32	Feb 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	33	Feb 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	34	Feb 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT

10726550a.trn

MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8  
NEWS X25 X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 14:41:45 ON 10 MAR 2007

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:41:54 ON 10 MAR 2007

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2007 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 MAR 2007 HIGHEST RN 925981-65-3

DICTIONARY FILE UPDATES: 9 MAR 2007 HIGHEST RN 925981-65-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

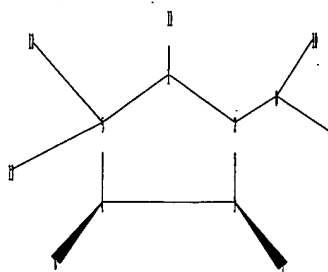
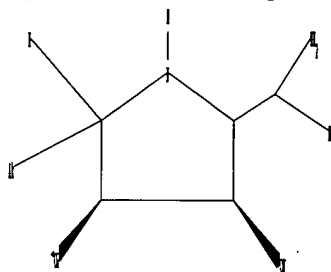
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

10726550a.trn

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10726550a.str



chain nodes :  
6 7 8 9 10 11 12 13  
ring nodes :  
1 2 3 4 5  
chain bonds :  
1-11 2-8 3-7 4-6 5-12 5-13 8-9 8-10  
ring bonds :  
1-2 1-5 2-3 3-4 4-5  
exact/norm bonds :  
1-2 1-5 3-7 4-6 5-13 8-10  
exact bonds :  
1-11 2-3 2-8 3-4 4-5 5-12 8-9  
isolated ring systems :  
containing 1 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
10:CLASS 11:CLASS 12:CLASS 13:CLASS

Stereo Bonds:

6-4 (Single Wedge).  
7-3 (Single Wedge).

Stereo Chiral Centers:

3 (Parity=Odd)  
4 (Parity=Odd)

Stereo RSS Sets:

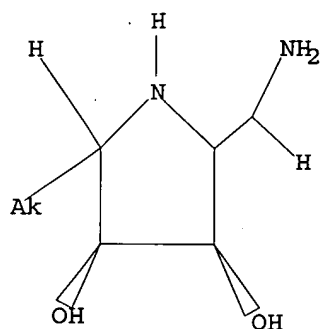
Type=Relative (Default). 2 Nodes= 3 4

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 14:42:09 FILE 'REGISTRY'  
 SAMPLE SCREEN SEARCH COMPLETED - 108 TO ITERATE

100.0% PROCESSED 108 ITERATIONS  
 SEARCH TIME: 00.00.01

1 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 1537 TO 2783  
 PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 14:42:16 FILE 'REGISTRY'  
 FULL SCREEN SEARCH COMPLETED - 2069 TO ITERATE

100.0% PROCESSED 2069 ITERATIONS  
 SEARCH TIME: 00.00.01

9 ANSWERS

L3 9 SEA SSS FUL L1

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
172.10	172.31

FULL ESTIMATED COST

FILE 'HCAPLUS' ENTERED AT 14:42:21 ON 10 MAR 2007  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing

10726550a.trn

of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 10 Mar 2007 VOL 146 ISS 12  
FILE LAST UPDATED: 9 Mar 2007 (20070309/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 3 L3

=> d l4 ibib abs hitstr tot

L4 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1060932 HCAPLUS

DOCUMENT NUMBER: 144:6996

TITLE: Stereoselective synthesis of (2S,3S,4R,5S)-5-methylpyrrolidine-3,4-diol derivatives that are highly selective  $\alpha$ -L-fucosidase inhibitors

AUTHOR(S): Moreno-Vargas, Antonio J.; Carmona, Ana T.; Mora, Federico; Vogel, Pierre; Robina, Inmaculada

CORPORATE SOURCE: Department of Organic Chemistry, Faculty of Chemistry, University of Seville, Seville, E-41071, Spain

SOURCE: Chemical Communications (Cambridge, United Kingdom) (2005), (39), 4949-4951

PUBLISHER: CODEN: CHCOFS; ISSN: 1359-7345  
Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:6996

AB N-Phenylaminomethyl benzimidazolyl moieties attached at C-2 of (2S,3S,4R,5S)-5-methylpyrrolidine-3,4-diol increase the potency and selectivity of the inhibitory activity of these systems towards  $\alpha$ -L-fucosidases.

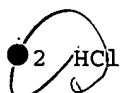
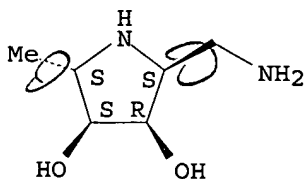
IT 869857-93-2P 869857-94-3P

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);  
BIOL (Biological study); PREP (Preparation)  
(stereoselective synthesis of methylpyrrolidinediol derivs. as selective  $\alpha$ -L-fucosidase inhibitors)

RN 869857-93-2 HCAPLUS

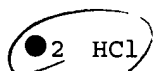
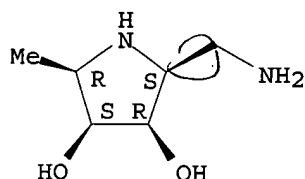
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-methyl-, dihydrochloride, (2S,3R,4S,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 869857-94-3 HCAPLUS  
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-methyl-, dihydrochloride,  
(2S,3R,4S,5R)- (9CI) (CA INDEX NAME)

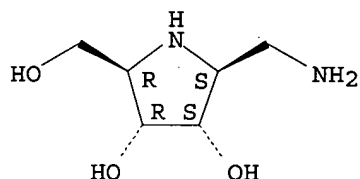
Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

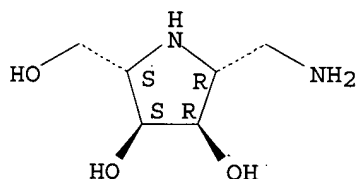
L4 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:400378 HCAPLUS  
DOCUMENT NUMBER: 141:38786  
TITLE: Syntheses and glycosidase inhibitory activities of  
2-(aminomethyl)-5-(hydroxymethyl)pyrrolidine-3,4-diol  
derivatives  
AUTHOR(S): Popowycz, Florence; Gerber-Lemaire, Sandrine; Schutz,  
Catherine; Vogel, Pierre  
CORPORATE SOURCE: Institute of Chemical Sciences and Engineering, Swiss  
Federal Institute of Technology, EPFL-BCH, Lausanne,  
CH-1015, Switz.  
SOURCE: Helvetica Chimica Acta (2004), 87(4), 800-810  
CODEN: HCACAV; ISSN: 0018-019X  
PUBLISHER: Verlag Helvetica Chimica Acta  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 141:38786  
AB New 2-(aminomethyl)-5-(hydroxymethyl)pyrrolidine-3,4-diol derivs. were  
synthesized from (5S)-5-[(trityloxy)methyl]pyrrolidin-2-one and their  
inhibitory activities toward glycosidases were evaluated. The influence  
of the configuration of the pyrrolidine ring on glycosidase inhibition was  
evaluated. (2R,3R,4S,5R)-2-[(benzylamino)methyl]-5-  
(hydroxymethyl)pyrrolidine-3,4-diol was a good and selective inhibitor of  
 $\alpha$ -mannosidase from jack bean ( $K_i = 1.2 \mu\text{M}$ ) and from almond ( $K_i =$   
 $1.0 \mu\text{M}$ ). Selectivity was lost for the non-benzylated derivative  
(2R,3R,4S,5R)-2-(aminomethyl)-5-(hydroxy-ethyl)pyrrolidine-3,4-diol which  
inhibited  $\alpha$ -galactosidases,  $\beta$ -galactosidases,  
 $\beta$ -glucosidases, and  $\alpha$ -N-acetylgalactosaminidase as well.  
IT 704901-91-7P 704901-99-5P 704902-18-1P  
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);  
BIOL (Biological study); PREP (Preparation)  
(syntheses from (5S)-5-[(trityloxy)methyl]pyrrolidin-2-one and  
glycosidase inhibitory activities of 2-(aminomethyl)-5-  
(hydroxymethyl)pyrrolidine-3,4-diol derivs.)  
RN 704901-91-7 HCAPLUS  
CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-(hydroxymethyl)-, (2S,3S,4R,5R)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



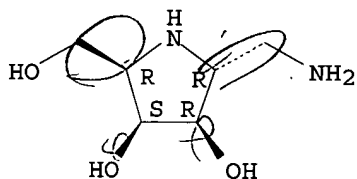
RN 704901-99-5 HCAPLUS  
 CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-(hydroxymethyl)-, (2R,3R,4S,5S)-  
 (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 704902-18-1 HCAPLUS  
 CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-(hydroxymethyl)-, (2R,3R,4S,5R)-  
 (9CI) (CA INDEX NAME)

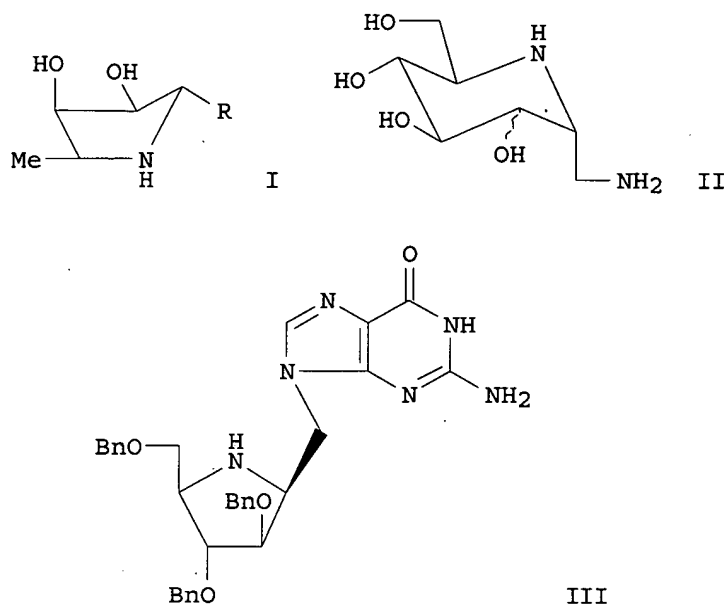
Absolute stereochemistry. Rotation (+).



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 1995:433855 HCAPLUS  
 DOCUMENT NUMBER: 122:291430  
 TITLE: Synthesis and Evaluation of Homoaza Sugars as  
 Glycosidase Inhibitors  
 AUTHOR(S): Wong, Chi-Huey; Provencher, Louis; Porco, John A.,  
 Jr.; Jung, Sang-Hun; Wang, Yi-Fong; Chen, Lihren;  
 Wang, Ruo; Steensma, Darryl H.  
 CORPORATE SOURCE: Department of Chemistry, Scripps Research Institute,  
 La Jolla, CA, 92037, USA  
 SOURCE: Journal of Organic Chemistry (1995), 60(6), 1492-501  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

GI



AB In an effort to develop transition-state mimetics of the glycosidase-catalyzed reaction, five- and six-membered azasugars and their homo-analogs were prepared and tested as inhibitors of glycosidases. Inhibition studies indicate that the fucosyl cation-like, five-membered imine and its reduced form I (R = H) are potent inhibitors of  $\alpha$ -fucosidase from bovine kidney with resp.  $K_i$  values of 160 nM and 2  $\mu$ M. The five-membered homoaminoaza sugar I (R = CH<sub>2</sub>NH<sub>2</sub>) is also a potent inhibitor of the enzyme ( $K_i = 1.9 \times 10^{-6}$  M), while the glucose and mannose-like six-membered homoaminoaza sugars II are less potent than the corresponding 1-deoxyaza sugars as inhibitors of  $\alpha$ -glucosidase and  $\alpha$ -mannosidase, resp. The primary amino group was placed in an attempt to introduce addnl. electrostatic interactions in the active site. The inhibitory activities are, however, in the high  $\mu$ M range. Synthesis of homoaza sugars structurally related to a disaccharide and a nucleoside III is also described.

IT 162895-60-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

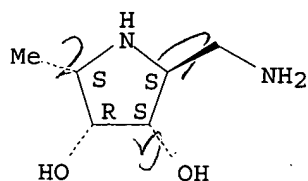
(synthesis and evaluation of homoaza sugars as glycosidase inhibitors)

RN 162895-60-5 HCAPLUS

CN 3,4-Pyrrolidinediol, 2-(aminomethyl)-5-methyl-, monohydrochloride, [2S-(2 $\alpha$ ,3 $\beta$ ,4 $\beta$ ,5 $\beta$ )]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





=> s azasugar

133 AZASUGAR

114 AZASUGARS

L5 199 AZASUGAR

(AZASUGAR OR AZASUGARS)

=> s l5 and sugar chain enzyme

258765 SUGAR

130958 SUGARS

330581 SUGAR

(SUGAR OR, SUGARS)

705584 CHAIN

315788 CHAINS

891260 CHAIN

(CHAIN OR CHAINS)

801089 ENZYME

464594 ENZYMES

1015619 ENZYME

(ENZYME OR ENZYMES)

3 SUGAR CHAIN ENZYME

(SUGAR (W) CHAIN (W) ENZYME)

L6 0 L5 AND SUGAR CHAIN ENZYME

=> s l5 and sugar chain

258765 SUGAR

130958 SUGARS

330581 SUGAR

(SUGAR OR SUGARS)

705584 CHAIN

315788 CHAINS

891260 CHAIN

(CHAIN OR CHAINS)

3123 SUGAR CHAIN

(SUGAR (W) CHAIN)

L7 1 L5 AND SUGAR CHAIN

=> s l5 and sugar

258765 SUGAR

130958 SUGARS

330581 SUGAR

(SUGAR OR SUGARS)

L8 70 L5 AND SUGAR

=> s l5 and configuration

10726550a.trn

293529 CONFIGURATION  
87370 CONFIGURATIONS  
353806 CONFIGURATION  
(CONFIGURATION OR CONFIGURATIONS)

L9 19 L5 AND CONFIGURATION

=> s l9 and py<=2001  
21882175 PY<=2001

L10 11 L9 AND PY<=2001

=> s l10 and enzyme  
801089 ENZYME  
464594 ENZYMES  
1015619 ENZYME  
(ENZYME OR ENZYMES)

L11 4 L10 AND ENZYME

=> d his

(FILE 'HOME' ENTERED AT 14:41:45 ON 10 MAR 2007)

FILE 'REGISTRY' ENTERED AT 14:41:54 ON 10 MAR 2007

L1 STRUCTURE UPLOADED

L2 1 S L1

L3 9 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 14:42:21 ON 10 MAR 2007

L4 3 S L3

L5 199 S AZASUGAR

L6 0 S L5 AND SUGAR CHAIN ENZYME

~~L7 1 S L5 AND SUGAR CHAIN~~

~~L8 70 S L5 AND SUGAR~~

L9 19 S L5 AND CONFIGURATION

L10 11 S L9 AND PY<=2001

L11 4 S L10 AND ENZYME

=> d l7 ibib abs hitstr tot

L7 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:76749 HCAPLUS

DOCUMENT NUMBER: 138:137514

TITLE: Preparation of azasugar compounds as  
specific inhibitors against sugar  
chain related enzymes

INVENTOR(S): Kanie, Osamu; Saotome, Chikako

PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan

SOURCE: BCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

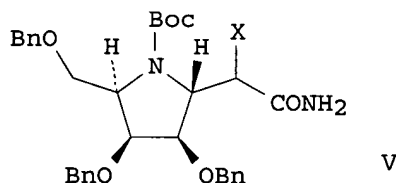
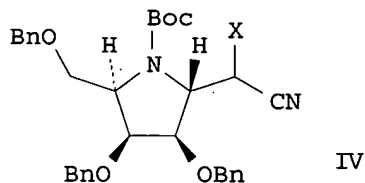
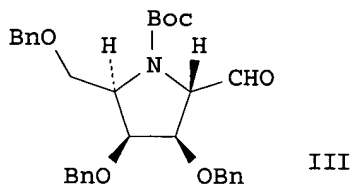
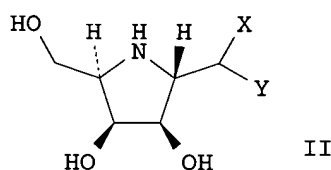
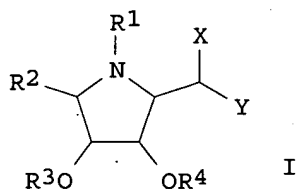
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008379	A1	20030130	WO 2002-JP5672	20020607
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,				

PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
 UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,  
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004147591 A1 20040729 US 2003-726550 20031204  
 PRIORITY APPLN. INFO.: JP 2001-173855 A 20010608  
 WO 2002-JP5672 A2 20020607  
 OTHER SOURCE(S): MARPAT 138:137514  
 GI



AB Compds. represented by the general formula (I) or salts thereof [wherein R1 is hydrogen, optionally substituted C1-10 alkyl, or an N-protecting group; R2 is optionally substituted C1-10 alkyl or optionally substituted C2-10 alkenyl; R3 and R4 are each independently hydrogen or a hydroxyl-protecting group; X is -N(R5)R6 or a residue derived from the amino group of an amino acid or a peptide (wherein R5 and R6 are each independently hydrogen, optionally substituted C1-10 alkyl, or optionally substituted C3-12 cycloalkyl); and Y is hydrogen, CH2NH2, CONH2, or CO2H] are prepared. These compds. are useful as specific inhibitors against sugar chain related enzymes including glycosyltransferase and glycosidase, and effective in the treatment or prevention of diseases in which sugar chain related enzymes participate. They also inhibit  $\alpha$ -GalNAc-ase (2-acetamido-2-deoxy- $\alpha$ -D-galactoside acetamidodeoxygalactohydrolase, an inactivation factor of macrophage activation factor) and thereby are useful as antiviral agents, anticancer agents, and immunostimulants. A small library of 27 iminocyclitols [II; X = BuNH, Me2NCH2CH2NH, Me(CH2)9NH, HOCH2CH2NH, 1-adamantylamino, MeO(CH2)3NH, tetrahydrofuran-2-ylmethylamino, phenethylamino, cyclohexylamino; Y = H, CH2NH2, CONH2] were prepared by (1) reductive amination of an aldehyde (III)

with various amines (e.g. phenethylamine) followed by deprotection and (2) Strecker reaction of the aldehyde with trimethylsilyl cyanide with various amines and Pd-catalyzed hydrogenolysis of the resulting amino nitriles (IV; X = same as above) or conversion of the amino nitriles IV into amino carboxamides (V; X = same as above) followed by Pd-catalyzed hydrogenolysis. The compds. II showed a broad spectrum of inhibitory activity against enzymes tested including  $\alpha$ -glucosidase,  $\alpha$ -mannosidase,  $\alpha$ -galactosidase,  $\beta$ -galactosidase, and  $\alpha$ -GalNAc-ase,  $\alpha$ -1,3-galactotransferase, and  $\beta$ -1,4-galactotransferase, but none of the compds. showed  $\alpha$ -glucosidase-inhibitory activity comparable to that of deoxynojirimycin. The structure-activity relationship for the enzyme inhibitory activity was also discussed.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l10 ibib abs hitstr tot

L10 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:30733 HCAPLUS

DOCUMENT NUMBER: 136:212683

TITLE:  $\alpha$ -Retaining glucosyl transfer catalysed by trehalose phosphorylase from Schizophyllum commune: mechanistic evidence obtained from steady-state kinetic studies with substrate analogues and inhibitors

AUTHOR(S): Nidetzky, Bernd; Eis, Christian

CORPORATE SOURCE: Institute of Food Technology, University of Agricultural Sciences Vienna (BOKU), Vienna, A-1190, Austria

SOURCE: Biochemical Journal (2001), 360(3), 727-736

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER: Portland Press Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fungal trehalose phosphorylase is classified as a family 4 glucosyltransferase that catalyzes the reversible phosphorolysis of  $\alpha,\alpha$ -trehalose with net retention of anomeric configuration. Glucosyl transfer to and from phosphate takes place by the partly rate-limiting interconversion of ternary enzyme-substrate complexes formed from binary enzyme-phosphate and enzyme- $\alpha$ -D-glucopyranosyl phosphate adducts resp. To advance a model of the chemical mechanism of trehalose phosphorylase, we performed a steady-state kinetic study with the purified enzyme from the basidiomycete fungus Schizophyllum commune by using alternative substrates, inhibitors and combinations thereof in pairs as specific probes of substrate-binding recognition and transition-state structure. Orthovanadate is a competitive inhibitor against phosphate and  $\alpha$ -D-glucopyranosyl phosphate, and binds 3 x 10<sup>4</sup>-fold tighter (K<sub>1</sub> 1  $\mu$ M) than phosphate. Structural alterations of D-glucose at C-2 and O-5 are tolerated by the enzyme at subsite + 1. They lead to parallel effects of approx. the same magnitude (slope = 1.14; r<sup>2</sup> = 0.98) on the reciprocal catalytic efficiency for reverse glucosyl transfer [log (K<sub>m</sub>/k<sub>cat</sub>)] and the apparent affinity of orthovanadate determined in the presence of the resp. glucosyl acceptor (log K<sub>i</sub>). An adduct of orthovanadate and the nucleophile/leaving group bound at subsite +1 is therefore the true inhibitor and displays partial transition state analogy. Isofagomine binds to subsite -1 in the enzyme-phosphate complex with a dissociation constant of 56  $\mu$ M and inhibits trehalose phosphorylase at least 20-fold better than 1-deoxynojirimycin.

The specificity of the reversible azasugars inhibitors would be explained if a pos. charge developed on C-1 rather than O-5 in the proposed glucosyl cation-like transition state of the reaction. The results are discussed in the context of  $\alpha$ -retaining glucosyltransferase mechanisms that occur with and without a  $\beta$ -glucosyl enzyme intermediate.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:845492 HCAPLUS

DOCUMENT NUMBER: 136:114658

TITLE: Biochemical and structural assessment of the 1-N-azasugar GalNAc-isofagomine as a potent family 20  $\beta$ -N-acetylhexosaminidase inhibitor

AUTHOR(S): Mark, Brian L.; Vocadlo, David J.; Zhao, Dalian; Knapp, Spencer; Withers, Stephen G.; James, Michael N. G.

CORPORATE SOURCE: Department of Biochemistry, Canadian Institutes of Health Research Group in Protein Structure and Function, University of Alberta, Edmonton, AB, T6G 2H7, Can.

SOURCE: Journal of Biological Chemistry (2001), 276(45), 42131-42137

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Azasugar inhibitors of the isofagomine class are potent competitive inhibitors of configuration-retaining  $\beta$ -glycosidases. This potency results from the formation of a strong electrostatic interaction between a protonated endocyclic nitrogen at the anomeric center of the inhibitor and the catalytic nucleophile of the enzyme. Although the majority of retaining  $\beta$ -glycosidases use a mechanism involving a carboxylate residue as a nucleophile, *Streptomyces plicatus*  $\beta$ -N-acetylhexosaminidase (SpHEX) and related family 20 glycosidases lack such a catalytic residue and use instead the carbonyl oxygen of the 2-acetamido group of the substrate as a nucleophile to attack the anomeric center. Thus, a strong electrostatic interaction between the inhibitor and enzyme is not expected to occur; nonetheless, the 1-N-azasugar (2R,3R,4S,5R)-2-acetamido-3,4-dihydroxy-5-hydroxy methyl-piperidinium hydrochloride (GalNAc-isofagomine·HCl), which was synthesized and assayed for its ability to inhibit SpHEX, was found to be a potent competitive inhibitor of the enzyme ( $K_i = 2.7 \mu\text{M}$ ). A crystallog. complex of GalNAc-isofagomine bound to SpHEX was solved and refined to 1.75 Å and revealed that the lack of a strong electrostatic interaction between the anomeric center of GalNAc-isofagomine and SpHEX is compensated for by a novel 2.8-Å hydrogen bond formed between the equatorial proton of the endocyclic nitrogen of the azasugar ring and the carboxylate of the general acid-base residue Glu-314 of SpHEX. This interaction appears to contribute to the unexpected potency of GalNAc-isofagomine toward SpHEX.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

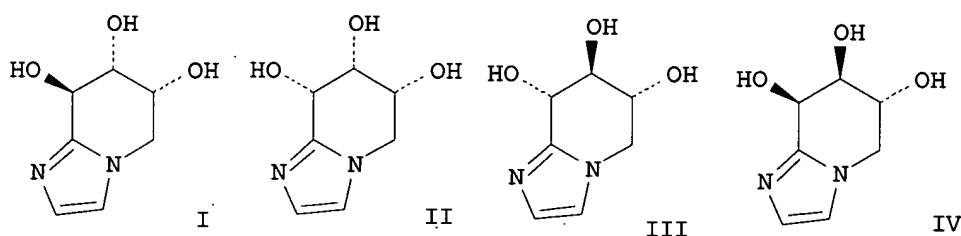
L10 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:830177 HCAPLUS

DOCUMENT NUMBER: 136:200356

TITLE: Carbohydrate transition state mimics, I Synthesis of

imidazolo-piperidinopentoses as nagstatine analogues  
 AUTHOR(S): Gessier, Francois; Tschamber, Theophile; Tarnus, Celine; Neuburger, Markus; Huber, Walter; Streith, Jacques  
 CORPORATE SOURCE: Ecole Nationale Supérieure de Chimie, Université de Haute-Alsace, Mulhouse, 68093, Fr.  
 SOURCE: European Journal of Organic Chemistry (2001), (21), 4111-4125  
 CODEN: EJOCFK; ISSN: 1434-193X  
 PUBLISHER: Wiley-VCH Verlag GmbH  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 136:200356  
 GI



AB The syntheses of the four imidazolo-piperidino-pentoses (I-IV), which belong to the D-series, and of their L-enantiomers, are reported. Ascorbic acid and isoascorbic acid were converted over several steps into the L-threo/L-erythro- and the D-erythro/D-threo-configured aldotetroses, resp., which are the key building blocks for the eight target imidazolo-pentoses cited above. Nucleophilic addition of a metalated imidazole to any one of these four aldotetroses gave the corresponding two diastereomeric adducts, intramol. cyclisation of which provided the expected bicyclic target mols., with some protection and deprotection steps being unavoidable prerequisites. The structures and configurations of all eight I-IV were determined unambiguously, by a combination of  $^1\text{H}/^{13}\text{C}$  NMR spectroscopy, CD (CD) and  $[\alpha]_D$  values, in conjunction with single-crystal X-ray diffraction analyses of the L-arabino and D-lyxo aza-sugars ent-3 and 6. Although lacking the hydroxymethylene group in the C(5) position, the overall structure of these eight stereomers strongly resembles that of the natural product nagstatine, a potent inhibitor of N-acetyl- $\beta$ -D-glucosaminidase. As a matter of fact, after examination of the inhibitory properties of these imidazolo-piperidinoses against six commonly encountered glycosidases, we observe that the L-arabino imidazolo-sugar ent-I is a potent inhibitor in this series, with  $K_i = 1 \mu\text{M}$  both with a  $\beta$ -glucosidase and with a  $\beta$ -galactosidase. The D-ribo and D-xylo stereomers II and III proved to be inhibitors of a  $\beta$ -glucosidase of similar magnitude (II:  $K_i = 20 \mu\text{M}$ ; III:  $K_i = 17 \mu\text{M}$ ), the other stereomers being either modest to poor inhibitors, or showing no inhibition at all.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2001:145753 HCAPLUS  
 DOCUMENT NUMBER: 134:193654  
 TITLE: Stereoselective synthesis of arabinose-derived phosphonates. [Erratum to document cited in

CA128:167630]  
AUTHOR(S): Bouix, Claire; Bissere, Philippe; Eustache, Jacques  
CORPORATE SOURCE: Laboratoire de Synthèse Organique et Chimie  
Microbienne Associée, Ecole Nationale Supérieure de  
Chimie de Mulhouse Associée au CNRS, Université de  
Haute-Alsace, Mulhouse, F-68093, Fr.  
SOURCE: Tetrahedron Letters (2000), 41(17), 3269  
CODEN: TELEAY; ISSN: 0040-4039  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The phosphonate 1 and its cyclic precursors (Scheme 1) all have the 2(R) configuration (instead of 2(S) as originally proposed). Accordingly, the carbamate 8 has the 2(S) configuration. The phosphonate 3 has the 2(S) configuration (instead of 2(R) as originally proposed).

L10 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:756196 HCAPLUS  
DOCUMENT NUMBER: 134:71806  
TITLE: A general approach to the synthesis of dideoxy and  
trideoxyiminoalditols from  $\beta$ -D-glycosides  
AUTHOR(S): Pistia, G.; Hollingsworth, R. I.  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Michigan  
State University, East Lansing, MI, 48824, USA  
SOURCE: Carbohydrate Research (2000), 328(4),  
467-472  
CODEN: CRBRAT; ISSN: 0008-6215  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 134:71806

AB Imino sugars (also called azasugars), a class of compds. of which the 1,5-dideoxy and 1,5,6-trideoxyiminoalditols are members, are important glycosidase inhibitors with very high potential as drugs. Their potential therapeutic applications range from the treatment of diabetes to cancer and AIDS. We present here a general method for the preparation of such compds. with the D-gluco and D-galacto configurations starting from  $\beta$ -D-glycosides. The procedure is especially appealing because of its high stereoselectivity and straightforwardness. The key steps are the selective oxidation of the glycosides to hexulosonic acids and reduction of the oxime derivs. to lactams, which are further reduced to the target compds. The C-6 position can be deoxygenated during the reduction if it bears an acetoxy group. Trideoxy imino sugars are then produced. Deacetylation prior to oxime reduction gives dideoxy compds.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:498609 HCAPLUS  
DOCUMENT NUMBER: 133:252629  
TITLE: A norbornyl route to azasugars: a new  
synthesis of deoxynojirimycin analogues  
AUTHOR(S): Mehta, G.; Mohal, N.  
CORPORATE SOURCE: Department of Organic Chemistry, Indian Institute of  
Science, Bangalore, 560 012, India  
SOURCE: Tetrahedron Letters (2000), 41(30),  
5741-5745  
CODEN: TELEAY; ISSN: 0040-4039  
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 133:252629  
AB A new synthesis of deoxynojirimycin (DNJ) analogs (galacto- and altro-configuration) has been achieved through a functionalized cyclopentene derivative crafted from the norbornyl system, employing double reductive amination as the key step. The new DNJ analogs have been evaluated against various glycosidases and found to be moderate to strong inhibitors.  
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2000:327708 HCAPLUS  
TITLE: General approach to the synthesis of imino-dideoxy and -trideoxy alditols from glycosides.  
AUTHOR(S): Pistia, Gabriela; Hollingsworth, Rawle I.  
CORPORATE SOURCE: Department of Chemistry, Michigan State University, East Lansing, MI, 48824, USA  
SOURCE: Book of Abstracts, 219th ACS National Meeting, San Francisco, CA, March 26-30, 2000 (2000), CARB-032. American Chemical Society: Washington, D. C.  
CODEN: 69CLAC  
DOCUMENT TYPE: Conference; Meeting Abstract  
LANGUAGE: English

AB Imino-sugars (also called azasugars) a class of compds. of which the 1,5-diimino-1,5-dideoxy and 1,5-diimino-1,5,6-trideoxy alditols are members, are important glycosidase inhibitors with very high potential as drugs. Their potential therapeutic applications range from the treatment of diabetes to cancer and AIDS. We present here a general method for the preparation of such compds. with the D-gluco and D-galacto configurations starting from glycosides. The procedure is especially appealing because of its high stereoselectivity and straightforwardness.

L10 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 1999:91214 HCAPLUS  
TITLE: Control of the anomeric configuration of bicyclic azasugars by remote substitution  
AUTHOR(S): Fan, Jianmei; Berges, David A.; Zhang, Na; Gonda, Shaun; Mower, Kendall  
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, 84602, USA  
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), CARB-054. American Chemical Society: Washington, D. C.  
CODEN: 67GHA6  
DOCUMENT TYPE: Conference; Meeting Abstract  
LANGUAGE: English

AB Most azasugars reported so far consist of either one ring or two rings which share a nitrogen atom and lack a heteroatom comparable to the glycosidic oxygen atom present in sugars. It is well known that glycosidases are exquisitely selective regarding the anomeric configuration of their substrates, and it appears that the selectivity of inhibition of glycosidases by azasugars with a glycosidic heteroatom can also be related to their anomeric configuration. As an approach to enhancing inhibitory selectivity, we have sought ways to control the anomeric configuration of azasugars which have an anomeric



heteroatom. Almost exclusive formation of a single anomeric product occurs when Me substituents are added to that ring of bicyclic azasugars which itself does not mimic a sugar. The synthesis and characterization of several examples will be described.

L10 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:39347 HCAPLUS

DOCUMENT NUMBER: 128:128209

TITLE: Conformation of 5-amino-5-deoxypentonolactams

AUTHOR(S): Kefurt, Karel; Havlicek, Jaroslav; Hamernikova, Michaela; Kerfurtova, Acenka; Votavova, Hana

CORPORATE SOURCE: Department Chemistry Natural Compounds, Prague  
Institute Chemical Technology, Prague, 166 28, Czech Rep.

SOURCE: Collection of Czechoslovak Chemical Communications (1997), 62(12), 1919-1930

CODEN: CCCCCA; ISSN: 0010-0765

PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Four configuration isomers of 5-amino-5-deoxy-D-pentonolactam and their tri-O-acetyl derivs. were studied using NMR and CD spectroscopy. For all compds. chemical shifts of the <sup>1</sup>H and <sup>13</sup>C nuclei as well as of vicinal coupling consts. were obtained. Comparison of the observed 3J(H,H) with those calculated for various conformations by a modified Karplus relationship led to the assignment of predominant conformation 3H<sub>4</sub>(D) or 4H<sub>3</sub>(D) to the lactams in solution. The most important factor for determining

the

conformation seems to be the pseudo-equatorial position of the substituent on the carbon next to the carbonyl group. The results of the CD spectra of the lactams in water, interpreted according to the currently used rules, agreed with the NMR results.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:727837 HCAPLUS

DOCUMENT NUMBER: 127:346586

TITLE: N-thiocarbonyl azasugars: a new family of carbohydrate mimics with controlled anomeric configuration

AUTHOR(S): Blanco, Jose L. Jimenez; Diaz Prez, Victor M.; Mellet, Carmen Ortiz; Fuentes, J.; Garcia Fernandez, Jose M.; Diaz Arribas, Juan C.; Canada, Francisco J.

CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Quimica, Universidad de Sevilla, Seville, E-41071, Spain

SOURCE: Chemical Communications (Cambridge) (1997), (20), 1969-1970

CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

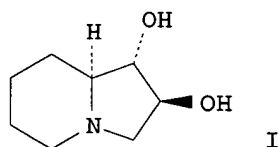
LANGUAGE: English

AB Bicyclic azasugar glycomimetics structurally related to the polyhydroxy-indolizine and -piperidine series incorporating a stereoelectronically controlled pseudoanomeric axial hydroxy group have been prepared by tautomeric rearrangement of cyclic thiocarbamate precursors; preliminary enzyme inhibition tests show an increased selectivity towards yeast  $\alpha$ -glucosidase for the  $\alpha$ -D-glucopyranose analog as compared with castanospermine or nojirimycin.

10726550a.trn

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 1995:833624 HCAPLUS  
DOCUMENT NUMBER: 123:314224  
TITLE: Assignment of the Absolute Configuration of Natural Lentiginosine by Synthesis and Enzymic Assays of Optically Pure (+) and (-)-Enantiomers  
AUTHOR(S): Brandi, Alberto; Cicchi, Stefano; Cordero, Franca M.; Frignoli, Roberta; Goti, Andrea; Picasso, Sylviane; Vogel, Pierre  
CORPORATE SOURCE: Dipartimento di Chimica Organica U. Schiff, Centro di studio C. N. R. sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, Florence, I-50121, Italy  
SOURCE: Journal of Organic Chemistry (1995), 60(21), 6806-12  
CODEN: JOCEAH; ISSN: 0022-3263  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 123:314224  
GI



AB The structure and absolute configuration of natural (+)-lentiginosine (I) isolated from plant sources was determined to be (1S,2S,8aS)-1,2-dihydroxyindolizidine on the basis of synthesis of both enantiomers and their inhibition of amyloglucosidases. (+)-I was derived from (L)-(+)-tartaric acid via a highly stereo- and regioselective 1,3-dipolar cycloaddn. of (3S,4S)-3,4-bis[(tert-butyldiphenylsilyl)oxy]-1-pyrroline N-oxide to methylenecyclopropane, followed by thermal rearrangement of the adduct into (1S,2S,8aS)-1,2-[(tert-butyldiphenylsilyl)oxy]octahydroindolizin-7-one. (-)-I was derived in the same way from (D)-(-)-tartaric acid. Both (+)-I and (-)-I displayed inhibition specificity for amyloglucosidases, being inactive toward 17 other glycosidases. With amyloglucosidase from *Aspergillus niger*, (+)-I displayed inhibition ( $K_i = 2 \mu\text{M}$ ) 5 times stronger than that reported for natural lentiginosine, 35 times that measured for (-)-I, and twice that of castanospermine. (+)-I is thus the most potent and specific competitive inhibitor of amyloglucosidases among azasugars and their analogs.

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:30733 HCAPLUS  
DOCUMENT NUMBER: 136:212683  
TITLE:  $\alpha$ -Retaining glucosyl transfer catalysed by trehalose phosphorylase from *Schizophyllum commune*:

mechanistic evidence obtained from steady-state kinetic studies with substrate analogues and inhibitors

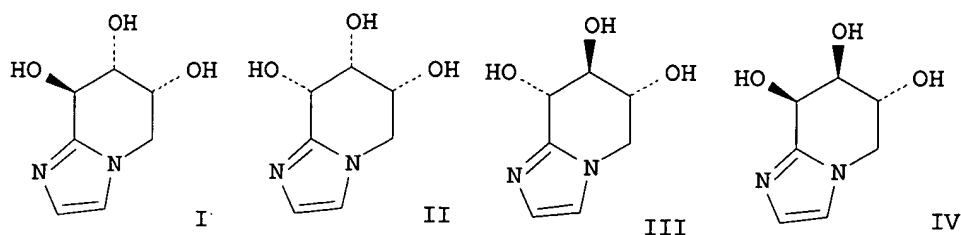
AUTHOR(S): Nidetzky, Bernd; Eis, Christian  
CORPORATE SOURCE: Institute of Food Technology, University of Agricultural Sciences Vienna (BOKU), Vienna, A-1190, Austria  
SOURCE: Biochemical Journal (2001), 360(3), 727-736  
CODEN: BIJOAK; ISSN: 0264-6021  
PUBLISHER: Portland Press Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Fungal trehalose phosphorylase is classified as a family 4 glucosyltransferase that catalyzes the reversible phosphorolysis of  $\alpha,\alpha$ -trehalose with net retention of anomeric configuration. Glucosyl transfer to and from phosphate takes place by the partly rate-limiting interconversion of ternary enzyme-substrate complexes formed from binary enzyme-phosphate and enzyme- $\alpha$ -D-glucopyranosyl phosphate adducts resp. To advance a model of the chemical mechanism of trehalose phosphorylase, we performed a steady-state kinetic study with the purified enzyme from the basidiomycete fungus *Schizophyllum commune* by using alternative substrates, inhibitors and combinations thereof in pairs as specific probes of substrate-binding recognition and transition-state structure. Orthovanadate is a competitive inhibitor against phosphate and  $\alpha$ -D-glucopyranosyl phosphate, and binds 3 x 10<sup>4</sup>-fold tighter (K<sub>i</sub> 1  $\mu$ M) than phosphate. Structural alterations of D-glucose at C-2 and O-5 are tolerated by the enzyme at subsite + 1. They lead to parallel effects of approx. the same magnitude (slope = 1.14; r<sup>2</sup> = 0.98) on the reciprocal catalytic efficiency for reverse glucosyl transfer [log (K<sub>m</sub>/k<sub>cat</sub>)] and the apparent affinity of orthovanadate determined in the presence of the resp. glucosyl acceptor (log K<sub>i</sub>). An adduct of orthovanadate and the nucleophile/leaving group bound at subsite +1 is therefore the true inhibitor and displays partial transition state analogy. Isogalactosamine binds to subsite -1 in the enzyme-phosphate complex with a dissociation constant of 56  $\mu$ M and inhibits trehalose phosphorylase at least 20-fold better than 1-deoxynojirimycin. The specificity of the reversible azasugars inhibitors would be explained if a pos. charge developed on C-1 rather than O-5 in the proposed glucosyl cation-like transition state of the reaction. The results are discussed in the context of  $\alpha$ -retaining glucosyltransferase mechanisms that occur with and without a  $\beta$ -glucosyl enzyme intermediate.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2001:845492 HCAPLUS  
DOCUMENT NUMBER: 136:114658  
TITLE: Biochemical and structural assessment of the 1-N-azasugar GalNAc-isogalactosamine as a potent family 20  $\beta$ -N-acetylhexosaminidase inhibitor  
AUTHOR(S): Mark, Brian L.; Vocadlo, David J.; Zhao, Dalian; Knapp, Spencer; Withers, Stephen G.; James, Michael N. G.  
CORPORATE SOURCE: Department of Biochemistry, Canadian Institutes of Health Research Group in Protein Structure and Function, University of Alberta, Edmonton, AB, T6G 2H7, Can.  
SOURCE: Journal of Biological Chemistry (2001),

276(45), 42131-42137  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Azasugar inhibitors of the isofagomine class are potent competitive inhibitors of configuration-retaining  $\beta$ -glycosidases. This potency results from the formation of a strong electrostatic interaction between a protonated endocyclic nitrogen at the anomeric center of the inhibitor and the catalytic nucleophile of the enzyme. Although the majority of retaining  $\beta$ -glycosidases use a mechanism involving a carboxylate residue as a nucleophile, *Streptomyces plicatus*  $\beta$ -N-acetylhexosaminidase (SpHEX) and related family 20 glycosidases lack such a catalytic residue and use instead the carbonyl oxygen of the 2-acetamido group of the substrate as a nucleophile to attack the anomeric center. Thus, a strong electrostatic interaction between the inhibitor and enzyme is not expected to occur; nonetheless, the 1-N-azasugar (2R,3R,4S,5R)-2-acetamido-3,4-dihydroxy-5-hydroxy methyl-piperidinium hydrochloride (GalNAc-isofagomine·HCl), which was synthesized and assayed for its ability to inhibit SpHEX, was found to be a potent competitive inhibitor of the enzyme ( $K_i = 2.7 \mu\text{M}$ ). A crystallog. complex of GalNAc-isofagomine bound to SpHEX was solved and refined to 1.75 Å and revealed that the lack of a strong electrostatic interaction between the anomeric center of GalNAc-isofagomine and SpHEX is compensated for by a novel 2.8-Å hydrogen bond formed between the equatorial proton of the endocyclic nitrogen of the azasugar ring and the carboxylate of the general acid-base residue Glu-314 of SpHEX. This interaction appears to contribute to the unexpected potency of GalNAc-isofagomine toward SpHEX.  
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  
L11 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2001:830177 HCAPLUS  
DOCUMENT NUMBER: 136:200356  
TITLE: Carbohydrate transition state mimics, I Synthesis of imidazolo-piperidinopentoses as nagstatine analogues  
AUTHOR(S): Gessier, Francois; Tschamber, Theophile; Tarnus, Celine; Neuburger, Markus; Huber, Walter; Streith, Jacques  
CORPORATE SOURCE: Ecole Nationale Supérieure de Chimie, Université de Haute-Alsace, Mulhouse, 68093, Fr.  
SOURCE: European Journal of Organic Chemistry (2001), (21), 4111-4125  
CODEN: EJOCFK; ISSN: 1434-193X  
PUBLISHER: Wiley-VCH Verlag GmbH  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 136:200356  
GI



AB The syntheses of the four imidazolo-piperidino-pentoses (I-IV), which belong to the D-series, and of their L-enantiomers, are reported. Ascorbic acid and isoascorbic acid were converted over several steps into the L-threo/L-erythro- and the D-erythro/D-threo-configured aldotetroses, resp., which are the key building blocks for the eight target imidazolo-pentoses cited above. Nucleophilic addition of a metalated imidazole to any one of these four aldotetroses gave the corresponding two diastereomeric adducts, intramol. cyclisation of which provided the expected bicyclic target mols., with some protection and deprotection steps being unavoidable prerequisites. The structures and configurations of all eight I-IV were determined unambiguously, by a combination of  $^1\text{H}/^{13}\text{C}$  NMR spectroscopy, CD (CD) and  $[\alpha]_D$  values, in conjunction with single-crystal X-ray diffraction analyses of the L-arabino and D-lyxo aza-sugars ent-3 and 6. Although lacking the hydroxymethylene group in the C(5) position, the overall structure of these eight stereomers strongly resembles that of the natural product nagstatine, a potent inhibitor of N-acetyl- $\beta$ -D-glucosaminidase. As a matter of fact, after examination of the inhibitory properties of these imidazolo-piperidinoses against six commonly encountered glycosidases, we observe that the L-arabino imidazolo-sugar ent-I is a potent inhibitor in this series, with  $K_i = 1 \mu\text{M}$  both with a  $\beta$ -glucosidase and with a  $\beta$ -galactosidase. The D-ribo and D-xylo stereomers II and III proved to be inhibitors of a  $\beta$ -glucosidase of similar magnitude (II:  $K_i = 20 \mu\text{M}$ ; III:  $K_i = 17 \mu\text{M}$ ), the other stereomers being either modest to poor inhibitors, or showing no inhibition at all.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:727837 HCAPLUS

DOCUMENT NUMBER: 127:346586

TITLE: N-thiocarbonyl azasugars: a new family of carbohydrate mimics with controlled anomeric configuration

AUTHOR(S): Blanco, Jose L. Jimenez; Diaz Prez, Victor M.; Mellet, Carmen Ortiz; Fuentes, J.; Garcia Fernandez, Jose M.; Diaz Arribas, Juan C.; Canada, Francisco J.

CORPORATE SOURCE: Departamento de Quimica Organica, Facultad de Quimica, Universidad de Sevilla, Sevilla, E-41071, Spain

SOURCE: Chemical Communications (Cambridge) (1997), (20), 1969-1970

CODEN: CHCOFS; ISSN: 1359-7345

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Bicyclic azasugar glycomimetics structurally related to the polyhydroxy-indolizine and -piperidine series incorporating a stereoelectronically controlled pseudoanomeric axial hydroxy group have

10726550a.trn

been prepared by tautomeric rearrangement of cyclic thiocarbamate precursors; preliminary enzyme inhibition tests show an increased selectivity towards yeast  $\alpha$ -glucosidase for the  $\alpha$ -D-glucopyranose analog as compared with castanospermine or nojirimicin.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
100.09	272.40

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-14.82	-14.82

CA SUBSCRIBER PRICE

STN INTERNATIONAL LOGOFF AT 14:51:07 ON 10 MAR 2007